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Constitut No Col

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February 8, 1994

FEDERAL EXPRESS
RETURN RECEIPT REQUESTED

Document Processing Center (TS-790) Office of Toxic Substances Environmental Protection Agency 401 M St. S.W. Washington, D.C. 20460

Attn: Section 8(e) Coordinator

Subject: TSCA Section 8(e) Submission

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OFFICE OF POLLUTION
C'LEVENTION AND TOXIC:
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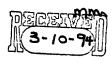
Dear Sir/Madam:

Elf Atochem North America Inc. is submitting the attached study to the Environmental Protection Agency (EPA) pursuant to Toxic Substances Control Act (TSCA) Section 8(e). This study provides information on Thioacetic acid (CAS No. 507-09-5) and does not involve effects in humans. The title of the enclosed study report is <u>Thioacetic acid Skin Sensitization Test in Guinea-Pigs</u>.

Nothing in this letter or the enclosed study report is considered confidential business information of Elf Atochem.

The following is a summary of the adverse effects observed in the skin sensitization test.

Thioacetic acid was tested for potential to produce allergic skin reaction by intradermal injection and akin application to guinea pigs using a modified Magnusson and Klingman method. The test material produced a 60% (14/20) sensitization rate and was classified as a moderate sensitizer.



TSCA 8(e) Submission Thioacetic acid February 8, 1994 Page 2

Elf Atochem has not previously filed any 8(e) notices or Premanufacture Notifications (PMNs) on the subject material.

Results from the study report will be incorporated into the current Elf Atochem Material Safety Data Sheet for Thioacetic acid.

Further questions regarding this submission may be directed to me at (215) 337-6892.

Sincerely,

C.H. Farr, PhD, DABT Manager, Product Safety and Toxicology

Enclosure

CIT

STUDY TITLE

SKIN SENSITIZATION TEST IN GUINEA-PIGS (Maximization method of Magnusson, B. and Kligman, A.M.)

TEST SUBSTANCE

THIOACETIC ACID

CENTRE INTERNATIONAL DE TOXICOLOGIE

SPONSOR

Elf Aquitaine Production
Usine de Lacq
64170 Artix
France

STUDY TITLE

SKIN SENSITIZATION TEST IN GUINEA-PIGS (Maximization method of Magnusson, B. and Kligman, A.M.)

TEST SUBSTANCE

THIOACETIC ACID

STUDY DIRECTOR
Jack Clouzeau

STUDY COMPLETION DATE
5th January 1994

PERFORMING LABORATORY

Centre International de Toxicologie (C.I.T.) Miserey - 27005 Evreux - France

LABORATORY STUDY NUMBER 10432 TSG

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| .CIT/Study No. | 10432 T | SG/THIOACETIC | ACID/Elf | Aquitaine | Production |
|----------------|---------|---------------|----------|-----------|------------|
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STATEMENT OF THE STUDY DIRECTOR

This study was performed in accordance with the protocol agreed upon by Elf Aquitaine Production, according to the maximization method of Magnusson and Kligman and according to:
. O.E.C.D. guideline No. 406, 12th May 1981.

The study was conducted in compliance with the principles of Good Laboratory Practice Regulations:

. O.E.C.D. Principles of Good Laboratory Practice, C(81)30(final) Annex 2. May 12, 1981.

I declare that this report constitutes a true and faithful record of the procedures undertaken and the results obtained in the performance of the study.

There were no influences, impacts or circumstances noted which might have impaired the integrity of this study.

This study was performed at the Centre International de Toxicologie (C.I.T.), Miserey, 27005 Evreux, France.

Toxicology

J. Clouzeau Biologist Date: 5.1.94

OTHER SCIENTISTS INVOLVED IN THIS STUDY

Pharmacy

J. Richard Doctor of Pharmacy

Toxicology

C. Pelcot Study Supervisor

STATEMENT OF THE QUALITY ASSURANCE UNIT

The protocol, study (main) and report were inspected by the C.I.T. Quality Assurance Unit on the following dates:

| Inspection | Date of inspection | Date of inspection report |
|----------------------------|--------------------|---------------------------|
| Protocol | 10.3.93 | 10.3.93 |
| Test substance/preparation | 28.9.93 | 28.9.93 |
| Report (first typing) | 22.12.93 | 22.12.93 |
| Report (final) | 5.1.94 | 5.1.94 |

The other stages (of the same type of studies) were inspected routinely on the following dates:

| Animals/housing | 8.9.93 | 8.9.93 |
|-----------------|--------|--------|
| Treatment | 3.9.93 | 3.9.93 |

The inspections were performed in accordance with C.I.T. procedures and the principles of Good Laboratory Practice Regulations.

M. Labiche

Date: 5.1.94

Pharmacist

Head of Quality Assurance Unit

and Scientific Archives

SUMMARY

At the request of Elf Aquitaine Production, Artix, France, the potential of the test substance, THIOACETIC ACID, to induce delayed contact hypersensitivity following intradermal injection and cutaneous application was evaluated in guinea-pigs according to the maximization method of Magnusson and Kligman and O.E.C.D. (No. 406, 12th May 1981). The study was conducted in compliance with the Principles of Good Laboratory Practice Regulations.

Methods

Thirty guinea-pigs (15 males and 15 females) were allocated to 2 groups: a control group 1 (5 males and 5 females) and a treated group 2 (10 males and 10 females).

The sensitization potential of the test substance was evaluated after a 10-day induction period during which time the animals were treated with the vehicle (control group) or the test substance (treated group). On day 1, in presence of Freund's complete adjuvant, 0.1 ml of the test substance at a concentration of 1% in the vehicle was administered by intradermal route. On day 8, 0.5 ml of the test substance at a concentration of 10% in the vehicle was applied by cutaneous route during 48 hours by means of an occlusive dressing. After a period of 12 days without treatment, a challenge cutaneous application of 0.5 ml of the vehicle (left flank) and 0.5 ml of the test substance at a concentration of 10% in the vehicle (right flank) were administered to all animals.

The test substance and the vehicle were prepared on a dry compress then were applied to the skin and held in place for 24 hours by means of an occlusive dressing. Cutaneous reactions on the challenge application sites were then evaluated 24 and 48 hours after removal of the dressing.

After the final scoring period, the animals were sacrificed and cutaneous samples were taken from the challenge application sites from all the animals. No histological examination was performed on the cutaneous samples.

The sensitivity of the guinea-pigs in C.I.T. experimental conditions were checked in a recent study with a positive sensitizer: Dinitro 2.4 Chlorobenzene. During induction period the test substance was applied at 0.05% (day 1) and 0.5% (day 8) concentrations. At cutaneous challenge application, 0.1% and 0.5% were tested on both flanks.

Results

No clinical signs and no deaths were noted during the study.

Sensitization skin reactions characterised by a well-defined and a moderate to severe erythema were observed after 24 hours on the right flank of 14/20 treated animals. No oedema was observed.

Inconclusive evidence of sensitization skin reactions (very slight erythema, score of 1) were noted in 6/20 treated animals.

After 48 hours, intensity of erythema reversed slightly. A dryness of the skin was noted after 48 hours in 19/20 treated animals. No oedema was observed.

The guinea-pigs which were used showed a satisfactory sensitization response in 100% animals using a positive sensitizer (appendix 5).

Conclusion

The test substance, THIOACETIC ACID, induced positive skin sensitization cutaneous reactions in 14/20 (60%) guinea-pigs. The allergenicity level of the test substance, THIOACETIC ACID, was moderate (III) in guinea-pigs.

1. INTRODUCTION

The objective of this study, performed according to maximization method established by Magnusson and Kligman (1), was to evaluate the potential of the test substance, THIOACETIC ACID, to induce delayed contact hypersensitivity in guinea-pigs.

The results of the study are of value in predicting the contact sensitization potential of the test material in Man.

During the induction period, the test substance was administered by intradermal route (together with an adjuvant to maximise potential reactions) and cutaneous route. After a rest period of 12 days, a challenge application with the test substance was performed in order to provoke a cutaneous sensitization reaction.

The study was conducted in compliance with: O.E.C.D. guideline No. 406, 12th May 1981.

2. MATERIALS AND METHODS

2.1. TEST AND CONTROL SUBSTANCES

2.1.1 Test substance

The test substance, THIOACETIC ACID, used in the study was supplied by Elf Aquitaine Production.

Documentation supplied by the Sponsor identified the test substance as follows:

- . denomination: THIOACETIC ACID
- . batch number: D 60018
- . labelling: ACIDE THIOACETIQUE; Lot D 60018; N° d'archivage au CAL: 1028/93
- . description: colourless liquid
- . container: a glass flask
- . date of receipt: 25.3.93
- . storage conditions: room temperature, protected from light
- . purity: 99.78%

During the study, liquid test substance was orange/yellow coloured.

Data relating to the characterization of the test substance are documented in a test article description and a certificate of analysis (presented in appendix 1) provided by the Sponsor.

21.2 Vehicle

The vehicle used was paraffin oil, batch No. 4747 (Coopérative Pharmaceutique Française, 77000 Melun, France).

(1) Magnusson, B.; Kligman, A.M.: The identification of contact allergens by animal assay. The guinea-pig maximization test. J. Invest. Derm. <u>52</u>: 268-276 (1969).

2.1.3 Other substances

The other substances used were:

- . sterile isotonic aqueous NaCl solution, batch No. 3019 (Biosédra, 92240 Malakoff, France);
- . Freund's complete adjuvant, batch No. 29829 (Osi, 75739 Paris, France);
- . sodium laurylsulphate, batch No. 112H0485 (Aldrich, 67000 Strasbourg, France);
- vaseline, batch No. 3006 (Monot, 21801 Quétigny, France).

2.2. TEST SYSTEM

2.2.1 Animals

Species and strain: Dunkin-Hartley guinea-pigs.

Reason for this choice: species recommended by the international regulations for sensitization studies. The strain used has been shown to produce a satisfactory sensitization response using known positive sensitisers.

Breeder: Centre d'Elevage Lebeau, 78950 Gambais, France.

Number: 30 animals (15 males and 15 females).

Allocation of the animals to the groups: on day -1, the animals were weighed and randomly allocated to 2 groups: a control group 1 consisting of 10 animals (5 males and 5 females) and a treated group 2 consisting of 20 animals (10 males and 10 females).

Weight: on day 1, the animals had a mean body weight of 410 ± 22 g for the males and 404 ± 23 g for the females.

Acclimatization: at least 5 days before the beginning of the study.

Identification of the animals: the animals were identified individually by an ear-tattoo.

2.2.2 Environmental conditions

During the acclimatization period and throughout the study, the conditions in the animal room were as follows:

. temperature: 22 ± 3°C . relative humidity: 50 ± 20% . light/dark cycle: 12 h/12 h

The air was non-recycled and filtered.

During the acclimatization period and throughout the study, the animals were housed individually in polycarbonate cages (48 x 27 x 20 cm) equipped with a polypropylene bottle. Sifted and dusted sawdust was provided as litter (SICSA, 92142 Alfortville, France). An analysis of potential residues and major contaminants is performed periodically (Laboratoire Wolff, 92110 Clichy, France).

2.2.3 Food and water

During the study, the animals had free access to "Guinea-pigs sustenance reference 106 diet" (U.A.R., 91360 Villemoisson-sur-Orge, France).

Food was periodically analysed (composition and contaminants) by the supplier.

The diet formula is presented in appendix 2.

Drinking water filtered by a F.G. Millipore membrane (0.22 micron) was contained in bottles. Bacteriological and chemical analysis of the water and detection of possible contaminants (pesticides, heavy metals and nitrosamines) are performed periodically. Results are archived at C.I.T.

There were no contaminants in the diet, water or sawdust at levels likely to have influenced the outcome of the study.

2.3. TREATMENT

2.3.1 Preliminary test

A preliminary test was performed to define the concentration to be tested in the main study.

By intradermal route

Determination of the Minimum Irritant Concentration (M.I.C.):

- . 24 hours before treatment, the dorsal region of the animals was clipped,
- . the test substance was prepared in an appropriate vehicle,
- intradermal administration of the test substance (volume 0.1 ml) at increasing concentrations was performed in order to determine the maximum concentration which does not cause necrosis or ulceration, but a slight irritation (2 concentrations per animal),
- . evaluation of the potential cutaneous reactions, 24 and 48 hours after injection.

By cutaneous route

Determination of the Minimum Irritant Concentration (M.I.C.) and Maximum Non-Irritant Concentration (M.N.I.C.):

- . 24 hours before treatment, the dorsal region of the animals was clipped,
- . if necessary the test substance was suspended in an appropriate vehicle,
- . 0.5 ml of each concentration was applied to a gauze patch of approximately 4 cm² and then held in place by an occlusive dressing for 24 hours (2 concentrations per animal),
- potential cutaneous reactions were evaluated 24 hours after removal of the gauze patches.

2.3.2 Main study

2.3.2.1 Preparation of the animals

For all animals and before each treatment, the application sites were:

- . clipped on days -1 and 7 (scapular area 4 x 2 cm),
- . clipped again on days 21 and 25 (each flank 2 x 2 cm) and shaved on day 21.

2.3.3 Induction phase by intradermal and cutaneous routes

2.3.3.1 Intradermal route

On day 1, 6 intradermal injections were made into a clipped area (4 x 2 cm) in the scapular region, using a needle (diameter: 0.50 x 16 mm, Terumo: C.M.L., 77140 Nemours, France) mounted on a 1 ml glass syringe (0.01 ml graduations, Record: Carrieri, 75005, Paris, France). Three injections of 0.1 ml were injected into each side of the animal, as follows:

Control group (figure 1)

- . Freund's complete adjuvant diluted to 50% with an injectable isotonic solution (NaCl 0.9%),
- . vehicle.
- . a mixture of 50/50 (v/v) Freund's complete adjuvant diluted to 50% with a sterile isotonic aqueous NaCl solution and the vehicle.

Treated group (figure 2)

- . Freund's complete adjuvant diluted to 50% with a sterile isotonic aqueous NaCl solution,
- . test substance at a concentration of 1% in the vehicle,
- . a mixture of 50/50 (v/v) Freund's complete adjuvant diluted to 50% with a sterile isotonic aqueous NaCl solution, and, the test substance at a concentration of 1% in the vehicle.

2.3.3.2 Cutaneous route

On day 7, the scapular area was clipped. As the test substance is shown to be non-irritant after occlusive cutaneous treatment during preliminary test, the animals were treated with 0.5 ml of sodium laurylsulphate (10%) in vaseline to provoke local irritation.

On day 8, a cutaneous application on the 6 injection areas (4 x 2 cm) of the scapular region was performed.

Control group

. application of 0.5 ml of the vehicle.

Treated group

. application of 0.5 ml of the test substance 10% in the vehicle.

The test substance and the vehicle were prepared a dry compress (Semes France, 54183 Heille-court, France), which were then applied to the scapular region and held in place for 48 hours by means of an adhesive hypoallergic dressing (Laboratoires de Pansements et d'Hygiène, 21300 Chenove, France) and an adhesive anallergic waterproof plaster (Laboratoire des Professions Médicales, 92240 Malakoff, France).

No residual test substance was observed at removal of the dressing.

One hour after removal of the occlusive dressing, cutaneous reactions were recorded.

2.3.3.3 Challenge phase

On day 22, the animals from both groups received an application of 0.5 ml of the test substance at a concentration of 10% in the vehicle on the posterior right flank, and 0.5 ml of the vehicle on the posterior left flank. This application was performed using a 1 ml plastic syringe (0.01 ml graduations, Terumo: C.M.L., 77140 Nemours, France). The articles were prepared on a dry compress (Semes France, 54183 Heillecourt, France), then applied to the skin. The compress was held in contact with the skin for 24 hours of means by an occlusive, hypoallergic dressing (Laboratoires de Pansements et d'Hygiène, 21300 Chenove, France) and an adhesive anallergic waterproof plaster (Laboratoire des Professions Médicales, 92240 Malakoff, France).

No residual test substance was observed at removal of the dressing.

2.4. SCORING OF CUTANEOUS REACTIONS

Twenty-four and 48 hours after removal of the dressing from the challenge application site, the both flanks of the treated and control animals were observed in order to evaluate cutaneous reactions, according to the following scale:

Erythema and eschar formation

| . No erythema | 0 |
|---|---|
| . Very slight erythema (barely perceptible) | |
| . Well-defined erythema | 2 |
| . Moderate to severe erythema | 3 |
| Severe erythema (beet redness) to slight eschar formation (injuries in depth) | 4 |

Oedema formation

| . No oedema | 0 |
|---|---|
| . Very slight oedema (barely perceptible) | 1 |
| . Slight oedema (visible swelling with well-defined edges) | 2 |
| . Moderate oedema (visible swelling raised more than 1 millimetre) | |
| . Severe oedema (visible swelling raised more than 1 millimetre and extending | |
| beyond the area of exposure) | 4 |

Any other lesions were noted.

2.5. CLINICAL EXAMINATIONS

The animals were observed twice a day during the study in order to record clinical signs and to check for mortality.

2.6. BODY WEIGHT

The animals were weighed individually on the day of allocation into the groups, on the first day of the study (day 1) and then on days 8, 15 and 25.

2.7. PATHOLOGY

2.7.1 Necropsy

On day 25, after the 48-hour observation period, the animals were sacrificed by CO₂ inhalation in excess.

2.7.2 Cutaneous samples

On day 25, a skin sample was taken from the treatment sites of the posterior left and right flanks of all animals. The samples were preserved in 10% buffered formalin.

2.7.3 Microscopic examination

No histological examinations were performed.

2.8. DETERMINATION OF THE ALLERGENICITY LEVEL

treated animals show a positive reaction if macroscopic cutaneous reactions are clearly visible (erythema and/or oedema ≥ 2) and different from those of the control animals, or, if "doubtful" macroscopic reactions are confirmed at microscopic examination as being due to the sensitization process. Sensitization reactions are characterized at microscopic examination by basal spongiosis, reactional acanthosis of the epidermis and infiltration of mononucleated cells into the dermis (1).

(1) Duprat, P.; Delsaut. L.; Gradiski, D.; Lepage, M.: Investigations histo-pathologiques et cytologiques lors de la mise en évidence, chez le cobaye, d'une allergie cutanée de type retardé. Revue Méd. Vét. 127: 7, 1083-1101 (1976).

Determination of the allergenicity level

The allergenicity level of the test substance is calculated by comparing the number of animals showing positive reactions with the number of surviving treated animals at the end of the study.

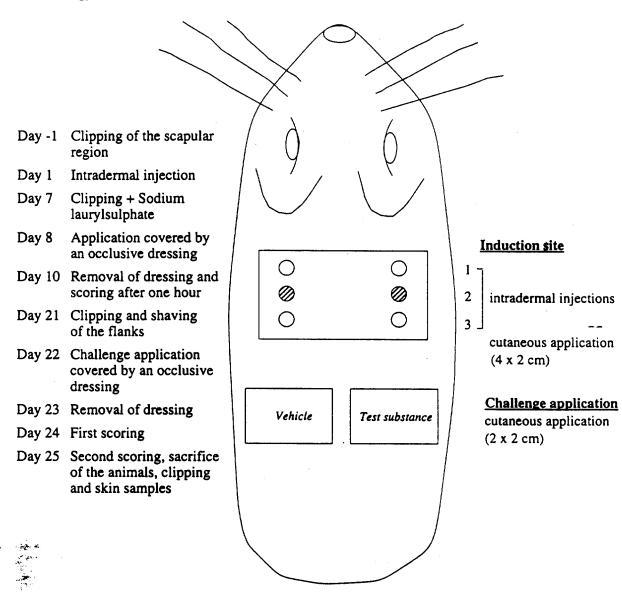
| • | Allergenicity level | Classification |
|---|------------------------|----------------|
| | I | very weak |
| | II | weak |
| | III | moderate |
| | IV | strong |
| | V | very strong |

According to the E.E.C. directive 91/325/E.E.C. published in the Journal Officiel des Communautés Européennes, when the reactions are positive in at least 30% of the treated animals, the test substance has sensitization properties and the sentence "R 43: May cause sensitization by skin contact" must be applied.

2.9. SUMMARY DIAGRAMS

Figure 1: control group

Chronology



2

vehicle

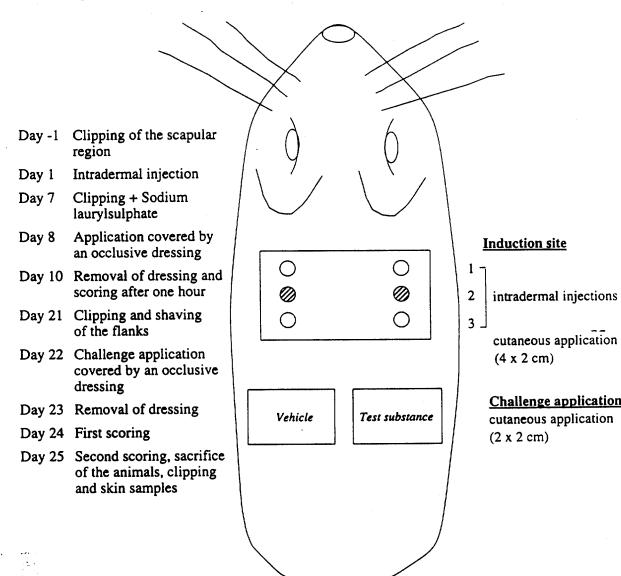
1 + 2,50/50 (v/v)

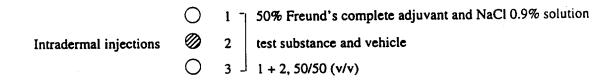
Intradermal injections

50% Freund's complete adjuvant and NaCl 0.9% solution

Figure 2: treated group

Chronology





2.10. CHRONOLOGY OF THE STUDY

The chronology of the study is summarized as follows:

| Procedure | Date | Day | |
|---|----------------------|----------|---|
| Arrival of the animals | 23.9.93 | -5 | _ |
| Allocation of the animals into groups | 27.9.93 | -1 | |
| Weighing, induction by intradermal injection | 28.9.93 | 1 | |
| Laurylsulfate application | 4.10.93 | 7 | |
| Weighing, induction by cutaneous route | 5.10.93 | 8 | |
| Removal of occlusive dressings and scoring of local reactions after 1 hour | 7.10.93 | 10 | |
| Weighing | 12.10.93 | 15 | |
| Challenge cutaneous application | 19.10.93 | 22 | |
| Removal of occlusive dressings | 20.10.93 | 23 | |
| Scoring of cutaneous reactions after . 24 hours . 48 hours | 21.10.93 22.10.93 | 24 25 | |
| Weighing, sacrifice of the animals and skin samples | 22.10.93 | 25 | |

2.11. ARCHIVES

The study archives:

- . protocol and possible amendments,
- . raw data,
- . correspondence,
- . final study report and possible amendments,
- . possible histological specimens:
 - tissues in preservative
- blocks
 - slides

are stored in the premises of C.I.T., Miserey, 27005 Evreux, France, for 5 years after the end of the *in vivo* study. At the end of this period, the study archives will be returned to the Sponsor.

3. RESULTS

3.1. PRELIMINARY STUDY

3.1.1 Administration by intradermal route

The maximal administrable concentration by intradermal route was 1% of the test substance in the vehicle in presence of Freund's complete adjuvant. Several tests were performed to determine the minimal irritant concentration which did not provoke necrosis or ulceration.

| Concentration of the test substance | Scoring aft | er treatment |
|-------------------------------------|-------------------|-------------------|
| % | 24 hours | 48 hours |
| 0.1 | slight irritation | slight irritation |
| 1 | irritation | irritation |

M.I.C. is $\geq 1\%$

Concentration used in the main study is 1% of the test substance.

3.1.2 Application by cutaneous route

The maximal applicable concentration by cutaneous route was 10% of the test substance in the vehicle. Several tests were performed to determine the M.I.C. and the M.N.I.C. after application of the test substance covered by an occlusive dressing for 24 hours.

| Concentration of the test substance % | Scoring 24 hours after removal of the dressing | | | |
|---------------------------------------|--|--|--|--|
| 1 | No cutaneous reactions (1) | | | |
| 10 | No cutaneous reactions (1) | | | |
| 100 | Severe erythema and signs of toxicity (2) | | | |

M.N.I.C. is 10% of the test substance.

M.I.C. was not determined.

- (1) No residual was observed.
- (2) Any residual were wipped off.

3.2. MAIN STUDY

3.2.1 Clinical examinations

No clinical signs or mortalities were observed during the study.

The body weight gain of the treated animals was normal when compared to that of the control animals (figures 3 and 4, appendix 3).

3.2.2 Scoring of cutaneous reactions (appendix 4)

3.2.2.1 End of the induction period

On day 10, after removal of the dressing irritation in the control and in the treated groups were observed at the intradermal injection sites.

3.2.2.2 Challenge application

After the challenge application, a very slight (1), well-defined (2), moderate to severe (3), erythema was observed at the following frequency:

Erythema

| Groups Sex | Sa., | Emithema | Scoring of the cutaneous parameters | | | | | |
|------------|----------------|------------------|-------------------------------------|----------------------|----------------------|------------------------------|--|--|
| | Erythema score | 24 hours | | 48 hours | | | | |
| | | LF | RF | LF | RF | | | |
| Control 1 | Male | 0 | 5/5 | 5/5 | 5/5 | 5/5 | | |
| Treated 2 | Male | 0 1 2 3 | 10/10 - - - | 2/10 6/10 2/10 | 10/10 - - - | 4/10 6/10 | | |
| Control 1 | Female | 0 | 5/5 | 5/5 | 5/5 | 5/5 | | |
| Treated 2 | Female | 0 1 2 3 | 10/10 - - - | 4/10 4/10 2/10 | 10/10 - - - | 2/10 5/10 1/10 2/10 | | |

LF: left flank (control) RF: right flank (treated)

No oedema was observed.

After the challenge application of the test substance, no cutaneous reactions were observed in the animals of the control group.

A positive response characterised by a well-defined and a moderate to severe erythema were observed on the right flank of 14/20 and 9/20 treated animals after 24 and 48 hours, respectively.

No oedema was noted.

Inconclusive evidence of sensitization skin reactions (very slight erythema, score of 1) were noted in 6/20 and 9/20 treated animals after 24 and 48 hours, respectively.

No erythema persisted after 48 hours in 2 animals. After 48 hours ,a dryness of the skin was noted in 19/20 treated animals.

4. CONCLUSION

The test substance, THIOACETIC ACID, induced positive skin sensitization cutaneous reactions in 14/20 (60%) guinea-pigs. The allergenicity level of the test substance, THIOACETIC ACID, was moderate (III) in guinea-pigs.

Figure 3: Male body weight gain (g)

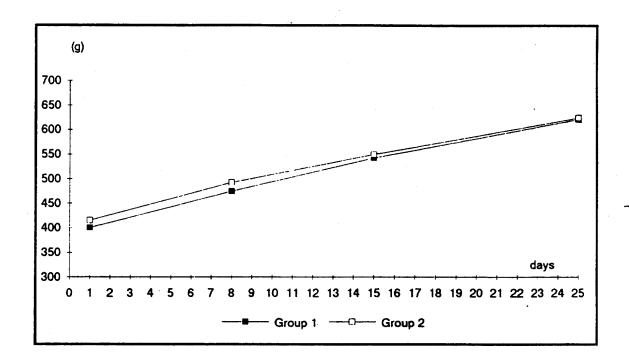
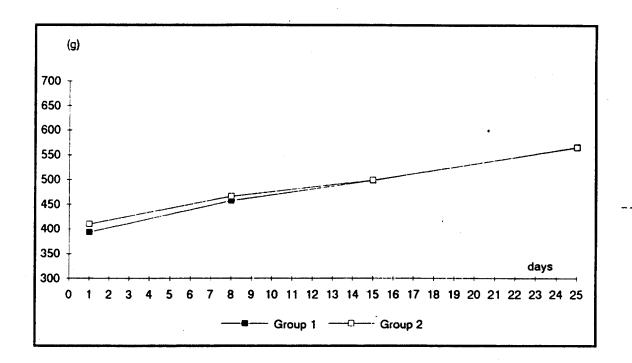


Figure 4: Female body weight gain (g)



APPENDICES

1. Test article description and certificate of analysis

TOXICOLOGY DEPARTMENT

CONFIDENTIAL ler March 1993

elf atochem s.a.

La défense 10, cedex 42 92091 Paris-la-Défense, France

TEST ARTICLE DESCRIPTION

THIOACETIC ACID

STRUCTURAL FORMULA

CH₃-COSH

IDENTITY

Test article name

: Thioacetic acid

Chemical name

: Ethanethioic acid

CAS number EINECS number

: 507-09-5 : 2080638

Molecular formula

: C₂H₄OS

Molecular weight

: 76.11

Purity Origin and batch : 99.78% (w/w) : SNEA(P), D 60018

Elf Atochem filing number

: CAL 1028/93

PHYSICAL AND CHEMICAL PROPERTIES

Appearance

: Colorless or clear yellow liquid

Viscosity

: 6.29 mPa.s at 20°C

Specific gravity

: 1.064-1.069 at 20°C

Melting point

: -17°C

Boiling point

: 87°C at 760 mm Hg (start of decomposition)

Vapor pressure

: 1.07 mbar at 20°C

Flash point

21°C (open cup)

Solubility Hydrolysis in water Soluble in DMSO

Soluble in ethylic alcohol

EXICOLOGICAL INFORMATIONS AND USE SAFETY

200 < LD50 / Oral / Rat < 400 mg/kg. Irritating to skin and eyes.

STORAGE AND DISPOSAL

Storage

: In dark and at room temperature

Expiry date

: March 1994

Disposal

Incineration

elf aquitaine production

adresse postale : BP 22 64170 Lacq téléphone : - 33 - 59 92 22 22 télex : pétra 560053F

direction exploration production france

CENTRE ATOCHEM LEVALLOIS

95 rue DANTON

92303 LEVALLOIS-PERRET

FRANCE

A l'attention de M. BOURALY

viréf.

n/réf.

93_6004

د و رويو کو چو

objet: ANALYSE de L'ACIDE THIOACETIQUE (ATA)

LOT D 60018

| CA | RACTERISTIQUES | ANALYSES |
|------------------|----------------|----------|
| Pureté | (%Poids) | 99.78 |
| Diacetyl sulfure | • | 0.15 |
| H2S | • | 0.56 |
| H2O | • | 0.02 |
| | | |

Lacq le 18 Février 1993

Elf Aquitaine Production société anonyme au capital de 1 055 000 000 F siège social : tour Elf. 2 place de la Coupole La Défense 6 Courbevoie (Hauts-de-Seine)

2. Diet formula



Ref: 106 COMPLETE DIET GUINEA-PIG MAINTENANCE DIET

Appearance: 4.5 mm diameter granules Conditioning: bags of 25 kgs

Daily portion: water ad libitum, Guinea-pigs 35-50 g.

| FORMULA % | |
|---|------|
| Cereals | 42 |
| Grain biproducts and legumes Vegetable protein (soya bean | 46 |
| meal, yeast) | 9 |
| Vitamin and mineral mixture | 3 |
| AVERAGE ANALYSIS % | |
| Calorific value (KCal/kg) | 2600 |
| Moisture | 10 |
| Proteins | 17 |
| Lipids | 3 |
| Carbohydrates (N.F.E.) | 49 |
| Fibre | 13 |
| Minerals (ash) | 8 |
| AMINO ACID VALUES | |
| (calculated in mg/kg) | |
| Arginine | 8500 |
| Cystine | 2500 |
| Lysine | 7200 |
| Methionine | 2100 |
| Tryptophan | 2000 |
| Glycine | 6000 |
| FATTY ACID VALUES | |
| (calculated in mg/kg) | |
| Palmitic acid | 3600 |
| Palmitoleic acid | 0 |
| Stearic acid | 700 |
| Oleic acid | |
| Linoleic acid | 1200 |
| Linolenic acid | 3000 |

| | MINERA Nat. | LS (calculat Input | ed in mg/kg) |
|----|----------------|-----------------------|--------------|
| | input | /MC | Total |
| P | 7400 | 1400 | 8800 |
| Ca | 5400 | 5600 | 11000 |
| K | 12000 | 0 | 12000 |
| Na | 1300 | 1950 | 3250 |
| Mg | 3270 | 130 | 3400 |
| Mn | 60 | 40 | 100 |
| Fe | 170 | 150 | 320 |
| Cu | 10 | 15 | 25 |
| Zn | 40 | 45 | 85 |
| Co | 0.1 | 1.5 | 1.6 |
| I | 0 | 0 | 0 |
| C1 | . 0 | 0 | 0 |

| VIT | AMINS (c | alculated pe | r kg) | |
|---------------|----------|--------------|----------|---|
| | Nat. | Synth. | | |
| | input | input | Total | |
| Vitamin A | 3500 IU | 7500 IU | 11000 IU | - |
| Vitamin D3 | 30 IU | 2000 IU | 2030 IU | |
| Vitamin B1 | 6 mg | 6.4 mg | 12.4 mg | |
| Vitamin B2 | 5 mg | 6.4 mg | 11.4 mg | |
| Vitamin B3 | 22 mg | 26 mg | 48 mg | |
| Vitamin B6 | 0.7 mg | 2.7 mg | 3.4 mg | |
| Vitamin B12 | 0.003 mg | 0.012 mg | 0.015 mg | |
| Vitamin C | 0 mg | 400 mg | 400 mg | |
| Vitamin E | 15 mg | 60 mg | 75 mg | |
| Vitamin K3 | 5 mg | 12.6 mg | 17.6 mg | |
| Vitamin PP | 97 mg | 14.5 mg | 111.5 mg | |
| Folic acid | 2.2 mg | 1.3 mg | 3.5 mg | |
| P.A.B. acid | 0 mg | 2.5 mg | 2.5 mg | |
| Biotin | 0.02 mg | 0.06 mg | 0.08 mg | |
| Choline | 1010 mg | 60 mg | 1070 mg | |
| Meso-Inositol | 0 mg | 62.5 mg | 62.5 mg | |
| L | | | | |

U.A.R., 7 rue Galliéni, 91360 Villemoisson - Tel: 69.04.03.57 - Fax: 69.04.81.97

This food is supplemented with stabilized coated vitamin C, avoiding the need of other food substances (greenery, ascorbic acid) if used within 4 months of date of manufacture.

3. Individual body weight values



INDIVIDUAL BODY WEIGHT VALUES
(g)

| Groups | Sex | Animals | Days | | | | | | | |
|-------------|--------|------------|------|-----|------|-----|-----|-----|-----|-----|
| | | | -1 | 1 | (1) | 8 | (1) | 15 | (1) | 25 |
| 1 | Male | 81 | 391 | 397 | 67 | 464 | 81 | 545 | 80 | 62 |
| | | 82 | 364 | 374 | 60 | 434 | 63 | 497 | 71 | 56 |
| | | 83 | 392 | 406 | 65 | 471 | 49 | 520 | 85 | 60 |
| | | 84 | 385 | 394 | 97 | 491 | 79 | 570 | 82 | 65: |
| | | 85 | 418 | 430 | 82 | 512 | 70 | 582 | 79 | 66 |
| | | М | 390 | 400 | 74 | 474 | 68 | 543 | 79 | 62 |
| | | SD | 19 | 20 | 15 | 29 | 13 | 35 | 5 | 38 |
| | Female | 96 | 370 | 386 | 84 | 470 | 33 | 503 | 64 | 56 |
| | | 97 | 423 | 425 | 30 | 455 | 76 | 531 | 46 | 57 |
| | | 98 | 398 | 402 | 47 | 449 | 9 | 458 | 77 | 53 |
| | | 99 | 345 | 356 | 89 | 445 | 61 | 506 | 74 | 580 |
| | | 100 | 380 | 396 | 70 | 466 | 27 | 493 | 78 | 57 |
| | | М | 383 | 393 | 64 | 457 | 41 | 498 | 68 | 56 |
| | | SD | 29 | 25 | 25 | 11 | 27 | 26 | 13 | 18 |
| 2 | Male | 86 | 406 | 412 | 84 | 496 | 52 | 548 | 84 | 63: |
| | | 87 | 430 | 456 | 76 | 532 | 44 | 576 | 80 | 65 |
| | | 88 | 399 | 408 | 78 | 486 | 49 | 535 | 68 | 60 |
| | | 89 | 376 | 385 | 75 | 460 | 53 | 513 | 68 | 58 |
| | | 90 | 394 | 405 | 46 | 451 | 55 | 506 | 52 | 55 |
| | | 91 | 410 | 426 | 101 | 527 | 75 | 602 | 70 | 673 |
| | | 92 | 374 | 380 | 72 | 452 | 46 | 498 | 73 | 57 |
| | | 93 | 418 | 431 | 86 | 517 | 72 | 589 | 103 | 692 |
| | | 94 | 410 | 419 | 70 | 489 | 66 | 555 | 60 | 615 |
| | | 95 | 419 | 432 | 85 | 517 | 59 | 576 | 94 | 670 |
| | | . M | 404 | 415 | 77 | 493 | 57 | 550 | 75 | 625 |
| | | SD | 18 | 23 | 14 | 31 | 11 | 36 | 15 | 47 |
| | Female | 101 | 383 | 389 | 50 | 439 | 41 | 480 | 98 | 578 |
| | | 102 | 399 | 406 | 47 | 453 | 40 | 493 | 53 | 546 |
| | | 103 | 370 | 376 | 54 | 430 | 29 | 459 | 59 | 518 |
| 200 - 10 | | 104 | 402 | 413 | 80 | 493 | 47 | 540 | 66 | 606 |
| 1 | | 105 | 413 | 423 | 45 | 468 | 58 | 526 | 56 | 582 |
| | | 106 | 419 | 438 | 62 | 500 | 51 | 551 | 73 | 624 |
| | | 107 | 395 | 396 | 72 | 468 | 35 | 503 | 77 | 580 |
| | | 108 | 382 | 393 | 50 | 443 | -60 | 383 | 102 | 485 |
| | | 109 | 421 | 437 | 63 | 500 | 33 | 533 | 44 | 577 |
| | | 110 | 420 | 428 | 40 | 468 | 55 | 523 | 33 | 556 |
| | | M | 400 | 410 | 56 | 466 | 33 | 499 | 66 | 565 |
| | | SD | 18 | 21 | - 13 | 25 | 34 | 50 | 22 | 41 |

^{(1) =} Body weight gain

M = Mean

SD = Standard Deviation

4. Individual observation of cutaneous reactions

MACROSCOPIC EXAMINATION OF CUTANEOUS REACTIONS Challenge application

| Group | Sex | Animals | | y 24 sco (after 2 hema RF | oring pe 4 hours Oed LF | riod) lema RF | | y 25 sc (after 4 thema RF | 48 hours | |
|---------|--------|----------|--------|------------------------------------|----------------------------------|-------------------------|--------|------------------------------------|----------|--------|
| Control | Male | 81 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| 1 | | 82 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | | 83 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | | 84 | .0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | | 85 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | Female | 96 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | | 97 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | | 98 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | | 99 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | | 100 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| Treated | Male | 86 | 0 | 1 | 0 | 0 | 0 | 2/S | 0 | 0 |
| 2 | | 87 | 0 | 2 | 0 | 0 | 0 | 2/S | 0 | 0 |
| | | 88 | 0 | 2 | 0 | 0 | 0 | 1/S | 0 | 0 |
| | | 89 90 | 0 | 3 | 0 | 0 | 0 | 2/S | 0 | 0 |
| | | 90 91 | 0 | 2 3 | 0 | 0 | . 0 | 2/S | 0 | 0 |
| | | 92 | 0 0 | 3 2 | 0 | 0 | 0 | 2/\$ | 0 | 0 |
| | | 93 | 0 | 1 | 0 0 | 0 | 0 | 1/S | 0 | 0 |
| | | 94 | 0 | 2 | 0 | 0 | 0 | 1/S | 0 | 0 |
| | | 95 | Ö | 2 | 0 | 0 | 0 0 | 2/S 1/S | 0 0 | 0 0 |
| | Female | 101 | 0 | | | • | _ | | | |
| | remaie | 101 | 0 0 | 1 2 | 0 | 0 | 0 | 1/S | 0 | 0 |
| | | 102 | 0 | 2 | 0 | 0 | 0 | 2/S | 0 | 0 |
| | | 103 | 0 | 2 | 0 | 0 0 | 0 | 1/S | 0 | 0 |
| | | 105 | 0 | 1 | 0 | 0 | 0 | 1/S 1/S | 0 | 0 |
| | | 106 | 0 | 1 | 0 | 0 | 0 | 1/S 0/S | 0 0 | 0 0 |
| , | | 107 | Ö | ì | ŏ | Ö | 0 | 0/S | 0 | 0 |
| ver", | | 108 | Ŏ | 2 | Ö | Ö | 0 | 1 | 0 | 0 |
| • | | 109 | ŏ | 3 | ŏ | Ŏ. | 0 | 3/S | 0 | 0 |
| | | 110 | Ö | 3 | ŏ | Ö | Õ | 3/S | 0 | 0 |

LF: left flank (control)
RF: right flank (treated)
S: dryness

5. Positive control to check the sensitivity of Dunkin-Hartley guinea-pigs

Purpose: check the sensitivity of Dunkin-Hartley guinea-pigs to a positive control test article

Method

Magnusson and Kligman

Test substance

DINITRO 2.4 CHLOROBENZENE

C.I.T. Study - Date

July 1993 (CIT/Study No. 10829 TPG)

Number of animals

5 females

Induction

0.05%

intradermal route day 1

0.5%

cutaneous route day 8

Challenge application:

0.1%

right flank

0.5%

left flank

Conclusion

In our experimental conditions and according to the Magnusson and Kligman method, DINITRO 2.4 CHLOROBENZENE at a concentration of 0.5% induced positive skin sensitization reactions in 100% of the guinea-pigs.

INDIVIDUAL REACTIONS: CHALLENGE PHASE MACROSCOPIC FINDINGS

| Const | | | 24-hour scoring period | | | 48-hour scoring period | | | | | | |
|---------|--------|---------|------------------------|------|-----|------------------------|------|------|-----|----|-------|-------|
| Group | Sex | Animals | | hema | Oed | iema | Eryt | hema | Oed | | Concl | usior |
| | | | LF | RF | LF | RF | LF | RF | LF | RF | LF | RF |
| Treated | Female | 16 | 3 | 2 | 0 | 0 | 3/S | 2/S | 0 | 0 | | |
| | | 17 | 3 | 2 | 0 | 0 | 3 | 1/S | ŏ | Õ | + | + |
| | | 18 | 4 | 2 | . 0 | 0 | 4 | 2/S | Ŏ | Õ | + | · |
| | | 19 | 4 | 2 | 0 | 0 | 4 | 1/S | 0 | Õ | + | + |
| | | 20 | 3 | 1 | 0 | 0 | 3/S | 0 | 0 | 0 | + | +/- |

₩-: bordeline

+ : hypersensitizing reaction

S: dryness of the skin

LF: left flank RF: right flank



UNITED STATES ENVIRONMENTAL PROTECTION AGENCY

WASHINGTON, D.C. 20460

C.H. Farr Manager, Product Safety and Toxicology Elf Altochem North America, Inc. 900 First Avenue, P.O. Box 1536 King of Prussia, Pennsylvania 19406-0018 PESTICIDES AND TOXIC SUBSTANCES

APR 1 2 1994

This letter formally acknowledges EPA's receipt of information submitted by your organization under Section 8(e), the "substantial risk" information reporting provision of the Toxic Substances Control Act (TSCA). For your reference, copies of the first page(s) of your submission(s) are enclosed and display the TSCA Section 8(e) Document Control Number (i.e., 8EHQ-0000-0000 Init.) assigned by EPA to your submission(s). Please refer to this cited number when submitting follow-up or supplemental information.

Please note that all submitted correspondence will be placed in the public files unless confidentiality is claimed according to the procedures outlined in Part X of EPA's TSCA Section 8(e) policy statement (43 FR 11110, March 16, 1978).

Confidential submissions submitted pursuant to the TSCA Section 8(e) Compliance Audit Program (CAP) should already contain information supporting confidentiality claims, because substantiation of CBI claims is required at the same time the 8(e) CAP is submitted to EPA. (If not done so already, please ensure that this information is provided to the Agency). When substantiating any/all claims, answer the questions detailed in the following attachment.

For NON-CAP submissions, any confidentiality claims should be supported by submission of information as described in the attachment(s).

12902 A

Trlage of 8(e) Submissions

| Date sent to triage: | · MAY 2 5 199/ | <u> </u> | (N | ON-CAP | CA | P |
|------------------------|---------------------|--------------|--------|----------------|------|-----|
| Submission number | 12902 | <u>A</u> | Ţ | SCA Inventory: | | N D |
| Study type (circle app | propriate): | | | | | |
| Group 1 - Dick Cleme | ents (1 copy total) | | | | | |
| ECO | AQUATO | | | | | |
| Group 2 - Erne Falke | (1 copy total) | | | | | |
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| Other (FATE, EXPO, M | ET, etc.): | | | | | |
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| CECATS/TRIAGE TRACKING DBASE ENTRY FORM INFORMATION REQUESTED: FLWP DATE: 0501 NO INFO REQUESTED (TECH) 0502 INFO REQUESTED (TECH) 0503 INFO REQUESTED (VOL ACTIONS) 0504 INFO REQUESTED (REPORTING RATIONALE) DISPOSITION: (639) REFER TO CHEMICAL SCREENING 0678 CAP NOTICE (64) CSRAD DATE: OBJUC 94 | 501 | INFORMATION TYPE: F C C C C C C C C C | SPECIES TOXICOLOGICAL CONCERN: G LOW MED HIGH DERMAL SE |
| SEO. A. C. | | F C | ONGOING REVIEW YES (DROP/REFER) NO (CONTINUE) REFER: |
| CECATS DATA: Submission # 8EHQ. 0294 - 12902 SEQ. A TYPE (INT.) SUPP FLWP SUBMITTER NAME: EIF ABOCHEM NOW-HD AMERICA INC. SUB. DATE: OZ 08 94 OTS DATE: OZ | CHEMICAL NAME: | INFORMATION TYPE: | TRIAGEDATA NON-CBI INVENTORY (YES) NO DETERMINE COMMENTS: Non - Cap |

8(E): 12902

HIGH - DERMAL SENSITIZATION

Dermal sensitization study in guinea pigs resulted in very slight, well-defined and moderate to severe erythema in 6/20, 10/20 and 4/20, respectively at 1st challenge. At 2nd challenge, 18/20 animals exhibited positive reactions.